Rare cancers group

Nat Rothman, Sholom Wacholder, Isis Mikhail

What is rare?

- **<15/100K, <40K cases in US per year**
- **NB: Children's cancers outside our mandate**

Rare cancers: annual cases and deaths

• Pancreas	31,860	31,270
• Uterine cervix	10,520	3,900
• Uterine corpus	40,320	7,090
• Ovary	25,580	16,090
• Vulva	3,970	850
• Testis	8,980	360
• Penis & other genital, male	1,570	270
• Kidney & renal pelvis	35,710	12,480
• Ureter, ther urinary organs	2,450	690
• Bones & joints	2,440	1,300
• Soft tissue (including heart)	8,680	3,660
• Brain	18,400	12,690
• Endocrine system	25,520	2,440
• Thyroid	23,600	1,460
• Hodgkin's disease	7,880	1,320
• Multiple myeloma	15,270	11,070
• Leukemia	33,440	23,300
• Non-Hodgkin's lymphoma	53,370	19,410

Why study rare tumors?

- Some are highly lethal
- Some have rising rates
- May be informative about etiology of more common tumors
- N. Risch: “lower incidence tends to go with more heritability (lambda)”
- Simpler etiology than common cancers?
  - e.g., RB, angiosarcoma, clear cell ca of vagina
- Disproportionate in some ethnic groups
- YPLL from cancer at young age
- Total incidence of all rare tumors is substantial

Rationale for study first study of a rare tumor

- Compare with study # 101 of a common tumor breast

How to study the etiology of rare tumors

- Gather data
  - Descriptive data from SEER
  - Existing cohorts
    - With and without biospecimens
    - Number of cases
    - Qx data available?
    - Biospecimen availability?
  - Existing clinical trials of rare tumors

Study design options-Cohorts

- Value to studies of modest size using existing cohorts
- Should be able to identify moderate to strong risk factors
  - Qx based analyses
  - Biologic samples
- How to obtain access to qx data and biologic samples?

Clinical trials

- Feasibility of adding etiology to tx trials of rare diseases
  - Precedent
    - Childhood cancer
  - Methodologic issues
    - e.g., Cases in trials may have worst prognosis
    - Yes, but …
    - We cannot afford to be overly fastidious
    - Strong apparent risk factors are robust to small biases

De novo designs

- **Why?**
  - **Follow up hypotheses from cohort mining**
  - **Functional assays/phenotypes from samples, fresh tissue**
  - **Subgroups with molecular categorization**
  - **Integrate with studies of prognosis and tx**

Basic design

- Study multiple kinds of rare tumors
- Hospital based
  - At major cancer centers
  - “that’s where the money is”
- Common hospital or clinic controls
- Single qx, biospecimen collection protocol
- Methodological challenges
  - Control selection
  - Surmountable

Building infrastructure

- Take advantage of GCRCs
- Supplemental funds to Cancer Centers to explore feasibility